The effect of stromal cell-derived factor-1alpha/heparin coating of biodegradable vascular grafts on the recruitment of both endothelial and smooth muscle progenitor cells for accelerated regeneration.

Journal: Biomaterials

Publication Year: 2012

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PubMed link: 22884813

Funding Grants: Interdisciplinary Training in Stem Cell Biology, Engineering and Medicine

Public Summary:
Small-diameter synthetic vascular grafts have high failure rate and tissue-engineered blood vessels are limited by the scalability. Here we engineered bioactive materials for vascular tissue engineering, which recruits two types of endogenous progenitor cells for the regeneration of blood vessels. Heparin was conjugated to microfibrous vascular grafts to suppress blood clotting, and stromal cell-derived factor-1alpha (SDF-1alpha) was immobilized onto heparin to recruit blood vessel progenitor cells. Heparin coating improved the short-term patency, and immobilized SDF-1alpha further improved the long-term patency of these engineered blood vessels when transplanted into animals. Grafts containing SDF-1alpha also effectively recruited progenitors of endothelial (blood-vessel lining) and smooth muscle cells, and showed superior elasticity. This in situ tissue engineering approach will have broad applications in regenerative medicine.

Scientific Abstract:
Small-diameter synthetic vascular grafts have high failure rate and tissue-engineered blood vessels are limited by the scalability. Here we engineered bioactive materials for in situ vascular tissue engineering, which recruits two types of endogenous progenitor cells for the regeneration of blood vessels. Heparin was conjugated to microfibrous vascular grafts to suppress thrombogenic responses, and stromal cell-derived factor-1alpha (SDF-1alpha) was immobilized onto heparin to recruit endogenous progenitor cells. Heparin-bound SDF-1alpha was more stable than adsorbed SDF-1alpha under both static and flow conditions. Microfibrous grafts were implanted in rats by anastomosis to test the functional performance. Heparin coating improved the short-term patency, and immobilized SDF-1alpha further improved the long-term patency. SDF-1alpha effectively recruited endothelial progenitor cells (EPCs) to the luminal surface of the grafts, which differentiated into endothelial cells (ECs) and accelerated endothelialization. More interestingly, SDF-1alpha increased the recruitment of smooth muscle progenitor cells (SMPCs) to the grafts, and SMPCs differentiated into smooth muscle cells (SMCs) in vivo and in vitro. Consistently, SDF-1alpha-immobilized grafts had significantly higher elastic modulus. This work demonstrates the feasibility of simultaneously recruiting progenitor cells of ECs and SMCs for in situ blood vessel regeneration. This in situ tissue engineering approach will have broad applications in regenerative medicine.